A FATAL CASE OF TAXUS POISONING

SEBASTIAN TRANCA, CRISTINA LAURA PETRISOR

Department of Anaesthesiology and Intensive Care, Iuliu Haţieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

Abstract

Context. *Taxine-derived alkaloids, taxane-derived substances, and glycosides seem to be responsible for the toxicity of Taxus spp. by blocking microtubule, sodium and calcium channels causing conduction abnormalities. Cases with Taxus baccata acute intoxication have rarely been reported.*

Case details. *We report the case of a 43-year-old man who ingested, for suicidal purposes, common (or European) yew leaves (Taxus baccata) and presented severe hypokalemia, ventricular arrhythmias with hemodynamic instability accompanied by severe multiple organ dysfunction syndrome, including respiratory insufficiency, renal failure, acid-base imbalance with severe hypokalemia, hepatic dysfunction and coma, which led to death 12 hours after Taxus baccata ingestion.*

Conclusion. *In this particular case, the cardiac electrical instability was definitely maintained by several causes, including severe hypokalemia, which has not been previously reported as related to Taxus poisoning. The metabolic acidosis associated with severe hypokalemia definitely contributed to the complex arrhythmias. The occurrence of severe hypokalemia needs further attention in cases with Taxus poisoning as its immediate treatment might increase survival chances.*

Keywords: European yew (Taxus baccata), intoxication, suicide.

Introduction

The European Yew (Taxus baccata, family: Taxaceae) is an evergreen poisonous coniferous tree. The cardiotoxic effects of the yew plant have been known for more than 2000 years [1]. The seeds, bark, and leaves of Taxus contain toxic compounds.

Lethal oral doses of yew leaves in humans are 0.6-1.3 g/kg, corresponding to 3.0-6.5 mg taxines/kg [2]. The taxoids are metabolized by liver enzymes and excreted into the bile [3]. Only a small portion is excreted in urine [4].

Taxine-derived alkaloids (e.g., taxine A and B, isotaxine B, paclitaxel), taxane-derived substances (e.g., taxol A and B), and glycosides (e.g., taxicatine) seem to be responsible for the toxicity of Taxus baccata. The general mechanism of action is the disruption of microtubule function [5]. Taxines e.g. taxine B block sodium and calcium channels, preferentially in cardiac myocytes, thus causing conduction abnormalities [6].

The first symptoms of taxus poisoning (nausea, vomiting, dizziness, diffuse abdominal pain, tachycardia, muscle weakness and confusion) begin after about one hour. These symptoms are followed by cardiovascular effects such as bradycardia, and then ventricular tachycardia with severe ventricular arrhythmias and episodes of ventricular fibrillation, severe hypotension and death [2].

Case report

A 43-year-old man, without coexisting disease, ingested for suicidal purposes common yew tree leaves (Taxus baccata), around 9:30 p.m. The family called the ambulance at 11:11 p.m. At their arrival the patient was obtunded (Glasgow coma scale 12 points), non-responsive, hemodynamically stable, with a BP of 110/60 mmHg, sinus rhythm, 86 beats/minute, 12 respirations/minute. One peripheral venous catheter was inserted, 500 ml of Ringer solution was administered and the monitored transport to the Emergency Department was performed.

At arrival in the Emergency Department (11:45 p.m.), the patient was comatose (GCS of 7 points), presented miosis. His blood pressure was 155/90 mm Hg, heart rate 115/min (sinus tachycardia with QRS waves of 0.13 seconds, QTc interval 0.36 seconds), no respiratory distress. The decision of rapid sequence intubation with Etomidate and Suxamethonium was made, considering

Manuscript received: 28.04.2013
Received in revised form: 22.08.2013
Accepted: 02.09.2013
Address for correspondence: tranca.sebastian@umfcluj.ro

airway protection. The patient was ventilated in SIMV mode (tidal volume 600 ml, imposed mandatory respiratory frequency 12/minute, with the persistence of 6 spontaneous breaths, PEEP 5 cm H_20, fraction of inspired oxygen (FiO_2) 60%). Blood was drawn for blood tests. A nasogastric tube was put in place after securing the airway and gastric lavage was performed with the evacuation of gastric contents with Tisa leaves. Activated charcoal was administered afterwards. A urinary catheter was put in place.

Abnormal initial laboratory values are presented in Table 1. Intravenous potassium replacement therapy was initiated (20 mEq/hour); 1000 ml Ringer solution was given and the gastric antisecretory therapy was started (Ranitidine 50 mg iv).

At 11:57 p.m. the patient presented pulseless ventricular tachycardia. CPR was initiated: the first 200 J biphasic electric shock was given right after the patient went into asystole. CPR maneuvers were continued (chest compressions, Epinephrine 1 mg i.v. every 3 minutes). The patient went from asystole into pulseless ventricular tachycardia, and a second 200J biphasic electric shock was given. 300 mg i.v. Amiodarone was administered after the third shock. After 20 minutes of CPR the patient presented central pulse, sinus tachycardia (120 b/min), widened QRS waves and blood pressure 60/40 mm Hg.

A central venous line was put in place (central venous pressure 12 cmH_2O) and inotropic support with Dopamine 15 micrograms/kg/min was initiated. Despite continuous support with increasing doses of dopamine, blood pressure values continued to deteriorate further and continuous infusion of Epinephrine was initiated, in increasing doses up to 10 micrograms/min. The patient presented anuria and acute kidney failure. He developed generalized seizures and 5 mg i.v. Diazepam was administered.

Table I. Laboratory results for the blood samples drawn in the ER (Emergency room) and ICU (Intensive care unit).

	ER (23p.m.)	ICU (5 a.m.)
Hb g/dl	15.3	14,2
Leukocytes	21.3	34.7
Platelets	220	224
Na mmol/l	137	140
K mmol/l	2.9	2.9
Ca mmol/l	0.7	0.8
glycemia mg/dl	243	200
urea mg/dl	51	66
creatinine mg/dl	1.1	1.7
GOT U/l	47	474
GPT U/l	20	184
LDH U/l	471	1050
amilase U/l	40	51
Total bilirubine mg/dl	0.6	1
CK U/l	170	267
CK-MB U/l	45	98
TQ sec	13	18
APTT sec	32	40
INR	1	1.5

The patient was transferred in the Intensive Care Department: comatose, intubated, with 8 spontaneous breaths being present, mechanically ventilated in SIMV mode (tidal volume 600 ml, mandatory respiratory frequency 14/minute, FiO_2 80%). Repeated laboratory values are presented in Table I. The blood gas analysis revealed metabolic acidosis: pH=7.21, PaO_2=68 mmHg, $PaCO_2$=39 mmHg, HCO_3^-=15, BE= -11, K=3 mEq/l, Ca=1.06 mEq/l, Cl=107 mEq/l, lactate 80 mg/dl; 100 ml $NaHCO_3$ was repeatedly administered. The patient continued to be hemodinamically unstable, blood pressure 60/45 mmHg, with decreasing heart rate (38 beats per min) for which i.v. Atropine 0.5 mg was repeatedly administered up to the total dose of 3 mg. The persistent low heart rate required immediate temporary external electrical pacing of the heart: demand mode, frequency of 60/min, intensity of 60 mA, with electrical and mechanical capture. After 30 minutes, the patient presented again ventricular fibrillation and CPR was again initiated, without favorable outcome. Time of death: 10 a.m.

Pulmonary congestion and edema, with eosinophilic contents of the alveoli, cerebral edema and enlarged liver with acute dystrophy were found on autopsy. Myocardial histopathological aspect revealed dilated vessels.

Discussion

Despite of its severe toxicity, fatal poisonings with Taxus spp. are rarely reported [6,7]. Most cases have been described in young subjects ingesting Taxus needles in suicidal intention [8]. As in the present case, the initial symptoms (nausea, vomiting, abdominal pains, dizziness) are followed by bradycardia, severe ventricular arrhythmias and episodes of ventricular fibrillation, severe hypotension and death.

Treatment is generally supportive. Orogastric lavage and the administration of activated charcoal limit further absorption of toxins from the gut. The development of hypotension, complete heart block, and bradycardia indicates a poor prognosis. In previous cases, the bradycardia has repeatedly been found to be refractory to transvenous cardiac pacing.[9] Considering the large volume of distribution of alkaloids extracted from Taxus (e.g. paclitaxel), and the physico-chemical properties of taxines (high molecular weight and relative water insolubility) [2], effective removal of taxines by haemodialysis appears unlikely. There are no data regarding the effectiveness of dyalisis in Taxus acute intoxication.

Our patient presented severe multiple organ dysfunction syndrome, including circulatory shock, respiratory insufficiency, renal failure, severe acid-base imbalance, hepatic dysfunction and coma, that resulted in the occurrence of death very soon after Taxus ingestion.

In our patient's case the electrical instability was not associated with prolonged QTc interval. The patient presented polymorphic ventricular tachycardia which is more often associated with long QTc interval. In this particular case, the cardiac electrical instability

was definitely maintained by several causes. The severe cardiogenic pulmonary oedema hampered resuscitation by generating hypoxemia. To our knowledge, severe hypokalemia has not been previously reported in case reports concerning Taxus poisoning. None of the clinical or laboratory parameters explained hypokalemia in our patient. The metabolic acidosis associated with severe hypokalemia definitely contributed to the complex arrhythmias in our case.

In conclusion, the occurrence of severe hypokalemia needs further attention in cases with Taxus poisoning as its immediate treatment might increase survival chances. Immediate and aggressive supportive treatment is necessary and all factors maintaining organ dysfunctions have to be addressed.

References

1. Wehner F, Gawatz O. Suizidale Eibenintoxikationen – von Casar bis heute – oder: Suizidanleitung im Internet. Arch Kriminol, 2003; 211:19-26.
2. Wilson CR, Sauer JM, Hooser SB. Taxines: a review of the mechanism and toxicity of yew (Taxus spp.) alkaloids. Toxicon, 2001; 39:175-185.
3. Monsarrat B, Alvinerie P, Wright M, et al. Hepatic metabolism and biliary excretion of Taxol in rats and humans. J Natl Cancer Inst Monogr, 1993; 15:39-46.
4. M. Suffness (Ed.). Taxol. Science and Applications, CRC Press, New York, 1995.
5. Fu Y, Li S, Zu Y, et al. Medicinal chemistry of paclitaxel and its analogues. Curr Med Chem, 2009; 16:3966-3985.
6. Willaert W, Claessens P, Vankelecom B, Vanderheyden M. Intoxication with Taxus Baccata: Cardiac arrhythmias following yew leaves ingestion. Pace, 2002; 25:511-512.
7. Van Ingen G, Visser R, Peitenburg H, Van Der Ark AM, Voortman M. Sudden unexpected death due to Taxus poisoning. A report of five cases, with review of the literature. Forensic Sci Int, 1992; 56:81-87.
8. Pietsch J, Schulz K, Schmidt U, Andresen H, Schwarze B, Dreßler J. A comparative study of five fatal cases of Taxus poisoning. Int J Legal Med, 2007; 121:417-422.
9. Von Der Werth J, Murphy JJ. Cardiovascular toxicity associated with yew leaf ingestion. Br Heart J, 1994; 72(1): 92-93.